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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/022,034	STROOBANT, PAUL	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-54* is/are pending in the application.

4a) Of the above claim(s) *12-16,18,21,22,49,51 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-11, 17, 19, 20, 23-48, 50, 52, 54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. NOTE the change of examiner in this application.

2. The amendment and the response filed on 7/29/05 has been fully considered and entered into the application.

Status of Claims

3. New claim 54 has been added and claim 2 has been canceled by the amendment.

4. Claims 1, 3-54 are currently pending in this application.

5. Claims 12-16, 18, 21-22, 49, 51 and 53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species election, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/26/04.

6. This application contains claims 12-16, 18, 21-22, 49, 51 and 53 drawn to an invention nonelected without traverse in Paper filed on 10/26/04. A complete reply to the final rejection must include cancellation of nonelected claims.

7. Claims 1, 3-11, 17, 19, 20, 23-48, 50, 52 and 54 are currently being examined in this application.

Maintained Claim Rejections

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. The rejection of Claims 1-11, 17, 19, 20, 23-48, 50 and 52 under 35 U.S.C. 112, second paragraph, set forth in the previous office action has been maintained for the reasons of record.

10. The lack of written description rejection of claims 1-11, 17, 19, 20, 23-48, 50 and 52 set forth in the previous office action has been maintained for the reasons of record.

11. The rejection of claims 1-11, 17, 19, 20, 23-27, 33-36, 42-48, 50 and 52 under 35 U.S.C. 102(b) as being anticipated by Cai et al. PNAS USA Vol. 92, pages 6537-6541 (July 1995) has been maintained for the reasons of record.

12. The rejection of claims 1-11, 17, 19, 20, 23-27, 29-48, 50 and 52 under 35 U.S.C. 103(a) as being unpatentable over Cai et al. PNAS USA Vol. 92, pages 6537-6541 (July 1995) and Hutchens et al. US Pat. No. 6,225,047 (5/01: effectively filed 6/97) has been maintained for the reasons of record.

13. The rejection of claims 1-11, 17, 19, 20, 23-48, 50 and 52 under 35 U.S.C. 103(a) as being unpatentable over Cai and Hutchens et al. as applied to claims 1-11, 17, 19, 20, 23-27, 29-48, 50 and 52 above, and further in view of Cull et al., Methods in Enzymology Vol. 182:147-238, has been maintained for the reasons of record.

New Rejections Necessitated by the Amendments

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

15. Claims 1, 3-11, 17, 19, 20, 23-48, 50, 52 and 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The amended claim 1 recites 'one or more first arrays comprising one or more

polypeptides from a first complex biological sample adhered to a support', it is not clear whether applicants mean that the 'one or more of the first arrays have the same peptide from the first biological sample' or have different peptides. Applicants are requested to clarify.

The amended claim 1 recites 'one or more second arrays comprising one or more polypeptides from a second complex biological sample adhered to a support', it is not clear whether applicants mean that the 'one or more of the second arrays have the same peptide from the second biological sample or have different peptides. Applicants are requested to clarify.

The amended claim recites in step e) 'exposing said peptide-nucleic acid library to one of said second array....' It is not clear whether the peptide-nucleic acid coupled library which is exposed to the first array in step c) is used again in the instant method step e) or does applicants mean that the members of the peptide-nucleic acid coupled library which do not bind or remain in the library or not utilized in step c) are used in step e).

The amended claim 1 recites ' first product comprising one or more species of said library that either (i) bind to said first array or (ii) do not bind to said first array.' Thus, the first product has either 'species' from the first array that which bind to the first array or the species, which do not bind to the first array. It is not clear what are the species in the library applicants referring to. Does applicants mean the 'Peptide nucleic acid' as species, or does applicants mean the members of the library. Further it is not clear what are the library members. Does applicants mean that the library has specific members, which are coupled to peptide nucleic acid (i.e., as tag or label). If the species of the library is considered as Pepetide- Nucleic acid, does applicants mean that the first product is the library members bound to the first array or unbound to the array. According to the specification, the members of the library which do not bind to the first

array (unbound members) are washed off, and only the members, which are bound to the first array were used in further assays. Applicants are requested to clearly recite which are considered as 'first product', 'second product', 'third product' or 'fourth product.'

The amended claim recites 'wherein the presence or absence of a species in said second or fourth product is indicative of identity of a polypeptide that is present in said first and second complex biological samples'. It is not clear how the presence and absence of a species in second and fourth product is indicative of a polypeptide. It is not clear how the presence of species of is an indicative of the polypeptide. Does applicants mean that the polypeptide is the species of the library. According to the claim 'second product comprises one or more species of first product (species of library which are bound to the first array or not bound to the first array) that either bind the second array or not bind to second array; and the presence or absence of a species in said second or fourth product is indicative of the identity of a polypeptide that is present in said first and second complex biological samples.'

For example if first array has protein A1 (A1, A1, A1), which is exposed to a library of protein B (B, B, B), and the product is considered as either A1-B (A1 bound to B) or A1 or B. The first product A1-B, A1 or B is exposed to second array A2 (A2, A2, A2) to result in a second product of A1-B-A2 (first product bound to the second array), A1-A2, B-A2 and B. In this example A1-A2 present in second product, thus A1-A2 is considered as polypeptide. But A1-A2 are not present in either first sample or second sample. Does applicants mean that the polypeptide of interest may be present in both first sample and second sample, that is A1 is same as A2. clarification is requested. Further, if the polypeptide is absent how is it identified from the claimed method is not clear.

According to the figure provided in page 13 of the response the 'bound phage is eluted' which is considered as first product, and the second product has non-bound phage. The applicant's response (and the figures) do not correspond to the claim limitations.

The amended claim also recites that 'not present in the same amount in said first complex biological sample compare to said second complex biological sample', it is not clear what amount is considered as same amount and further how is the relative concentration of the species would lead to identification of the polypeptide. Applicants are requested to clarify.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 5-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection.

The new limitations in claim 5 'providing one or more third arrays comprising one or more species from said amplified pooled product' has no clear support in the specification and the claims as originally filed. The subject matter claimed in claims 5-7-broadens the scope of the invention as originally disclosed in the specification.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

Response to Arguments

18. Claims 1-11, 17, 19, 20, 23-48, 50 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. In claim 1 (and claims dependent thereon), the phrase "adhering a complex biological sample ... to a support to create an array" is indefinite as to how one adheres the entire sample (vs. its individual components) to create an array. In this respect, the claimed method is incomplete.

b. In the claims (e.g. claims 1, 3, 5, 6, and claims dependent thereon), the metes and bounds of the chemical composition of "a first product", "a second product", "a third product", "fourth product" , "a fifth product" or a "a sixth product" is unclear. There are no definitions regarding this terminology nor do the examples provide sufficient guidance regarding the metes and bounds of this terminology. Do the products encompass peptidic, nucleic, saccharide etc. structure or a complex thereof.

c. Claims 1-11, 17, 19, 20, 23-48, 50 and 52 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omit ting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step identifying a polypeptide which is recited in the preamble (e.g. of claim 1) and a treating step (e.g. of claim 27) involving treatment of the "the complex biological sample".

19. Applicant's arguments filed on 7/29/05, regarding the rejection of claims under 35 USC, 112 second paragraph as being indefinite, have been fully considered but they are not persuasive.

Applicants amendments overcome the rejection a) in page 3 of the office action.

However, the rejections b) and c) have been maintained for the reasons of record.

Regarding rejection b) applicants argue that claims have been amended to clarify the composition of the products. However, it is still unclear what is considered as first product, second product, third product and fourth product.

Further, it is not clear whether these products are peptides, nucleic acids or the combination. Applicants response has not addressed these rejections.

Regarding rejection c, applicants assert that the amendments would clarify. However, the claim is still incomplete in view of the new rejections made in this office action. The amendments have not addressed the 'identifying step.'

20. Claims 1-11, 17, 19, 20, 23-48, 50 and 52 rejected less than 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (lack of adequate written description).

It is first noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co*

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)]. The *Lilly* court sets forth a two part test for written description: A description of a genus of cDNA's may be achieved by means of a recitation of:

1. a representative number of cDNA's, defined by nucleotide sequence, falling within the scope of the genus Or

2. of a recitation of structural features common to the members of the genus.

See *Regents of the University of California v. Eli Lilly & Co.* 119 F.3d 1559 (Fed. Cir. 1997) at 1569.

The present claims are directed to a method of identifying a polypeptide comprising exposing "peptide-nucleic acid coupled library" to various complex biological sample arrays from different "types of individuals" to generate "first/second/third/fourth/fifth/sixth" products. The claims fail to provide any structure or properties regarding the variously claimed "genera" of :

a. "peptide-nucleic acid coupled library";

b. "types of individuals" ; and/or

c. "first/second/third/fourth/fifth/sixth" products

nor does the specification provide any concrete definition thereof or representative examples thereof. The specification examples are directed to specific separation protocols involving phage library capture (e.g. complexation) of immobilized proteins derived from healthy/sick individuals.

In the present instance, neither the specification nor the claims provide:

1. A recitation of structural features common to the members of the various " genera" *OR*

2. a representative number of species representative of the various genera.

As pointed out in the above, neither the specification nor claims recite structural and/or functional features or provide a representative number of species to demonstrate possession of these claimed generics.

21. Applicant's arguments filed on 7/29/05, regarding the lack of written description rejection have been fully considered but they are not persuasive.

Applicants emphasize that the instant claims are directed to methods of identifying a polypeptide and not to compositions of matter per se.

Applicants seem to be asserting that 'the lack written description rejection is only applicable to compounds per se, and not to the methods.' Applicants arguments and assertions have been fully considered and are not persuasive.

Written description requirement of 35 USC. 112 exists independently of enablement requirement, and the requirement applies whether or not case involves question of priority, since requirement applies to all inventions including chemical inventions, and since the fact that patent is directed to method entailing use of compound, rather than to compound perse, does not remove

patentee's obligation to provide description of compound sufficient to distinguish infringing methods from non-infringing methods. See Univ. of Rochester v. G.D. Searle & Co., 358 F.3d 916, 920-23, 69 USPQ2d 1886, 1890-93 (Fed. Cir.2004).

Applicants further assert that one reading the specification can comprehend and practice the claimed methods, and it is the integral nature of the invention that the products of such screens can not be described in advance.

Applicants assertions are not persuasive, since the instant specification does not disclose the compounds encompassed by the 'peptide-nucleic acid coupled library', species of the products, first products, second products.' The specification discloses the phage display peptide libraries and methods of screening these peptide libraries with affinity columns comprising different samples, and identifying the peptides which bind to the affinity columns. The specification has not disclosed the arrays, the different products formed by contacting the sample adhered to the affinity columns and the PNA-coupled library. Note according the instant claimed method the peptide identified is either present or absent in both first and second complex biological samples. And there is no nexus between the presence or absence of species in second product or fourth product with the polypeptide identified.

Applicants further state that the facts of the instant case are similar to that of example 12 of Revised Interim Written guidelines training material promulgated in the office, and further state that the peptide-nucleic acid (PNA)coupled libraries are conventional in the art, and their use to identify the polypeptides in sample is conventional in the art. Thus, one skilled in the art would understand what is intended in the instant claim.

Applicants arguments are not persuasive. The Example 12 in the Guidelines is different from the instant claimed method. The Example 12 method does not disclose the limitations of two unknowns as in the instant claimed method (i.e., different number of arrays, and PNA-coupled libraries). Example 12 is drawn to selecting tissue specific compounds by comparing the quantity of expression (the level expression) in different tissues. Thus, based on level of expression the compounds specific to the tissue is identified. In this example, the compounds are known to be present in the various tissues in which the expression levels are being tested, which is different from the instant claimed method PNA-coupled libraries. The compounds in the instant PNA-coupled library have no known characteristics (no structure or function provided), and these unknown different compounds in the library are used to identify the presence of a polypeptide (may be known or unknown) in a complex biological sample array. Thus the claimed method is not similar to the example 12 of the Guidelines.

And the amendments to the claims to clarify the 'first through sixth products' do not overcome the issues under lack of written description. It is still not clear which compounds or species are present in the products. Does the products comprise the species which do not bind to the arrays, or which bind to the arrays? New claim 54 limitations are same as the deleted 'first and second type of individuals', i.e., diseased and healthy individual; or different species of animals. Thus, in view of the new rejections raised in this office action and the reasons of record the rejection has been maintained.

22. Claims 1-11, 17, 19, 20, 23-27, 33-36, 42-48, 50 and 52 are rejected under 35 U.S.C. 102(b) as being anticipated by Cai et al. PNAS USA Vol. 92, pages 6537-6541 (July 1995).

Present claim 1 is drawn to a method of identifying a polypeptide comprising:

a. adhering a "complex biological sample" from a first type of individual to a support to create an array;

b. adhering a complex biological sample from a second type of individual to a support to create an array;

c. exposing a "peptide-nucleic acid coupled library" at least one time to an array formed by step (a) to create a "first product"; and

d. exposing said first product at least one time to an array formed by step (b) to create a "second product".

Claim 2 reverses the order of claim 1 (e.g. by performing step b first and step a 2nd) to form "a third" and "fourth" product", respectively.

Claim 3 compares the "second" and "fourth" products respectively.

It is noted that the claims do not provide any structural or functional distinctions between the different recited products (e.g. first-sixth).

Cai et al. teach a method for identifying a "polypeptide" (e.g. antibodies or antigen markers) of normal vs tumor (e.g. melanoma) cells by adhering (e.g. culturing) "complex biological samples" (e.g. cells) from normal (e.g. healthy melanocytes) vs abnormal (e.g. tumor cells) which corresponds to steps a and b of present claim 1. Anti-melanoma antibodies were selected from each library by panning the phage against live cultures of the autologous tumor (e.g. from a "first type of individual" e.g. unhealthy) in which the complexed antibodies corresponding to a "first product". The panned phage population was extensively absorbed against normal melanocytes (e.g. "biological sample

from a second type of individual e.g. healthy) to enrich for antibodies that react with melanoma cells but not with melanocytes (e.g. unabsorbed antibody library as "second product") which anticipated present claims 1, 8-11, 17, 19, 20, 23-24 . The unabsorbed phage were amplified/cloned and tested (e.g. ELISA)against (e.g. exposing the library):

a. "a complex biological sample from a second type of individual (i.e. healthy such as normal endothelial and fibroblast cells) to identify antibodies that bind or those that don't (either of which corresponds to "a third product"); and

b. "a complex biological sample from a first type of individual (i.e. unhealthy such as melanocytes, several melanoma lines and eight other tumor lines) to identify antibodies that bind or those than don't (either of which corresponds to a "fourth product" but especially those that bind tumor antigens) thus anticipating present claims 2 (and claims dependent thereon). The reference teaches evaluating (e.g. ELISA) the test results of the above, including those of the "second" and "fourth" products (e.g. anticancer i.e. anti-melanoma antibodies) thus anticipating claim 3. The reference further teaches the identification (e.g. by ELISA) of different (e.g. three) classes of anti-melanoma antibodies from different patients; and the ***repeating of the above procedures*** utilizing the newly found anti-melanoma antibodies to screen the antibody repertoire of any person with cancer (or a person without cancer) which anticipates present claims 4-7 e.g. pooling and amplification of the product 2/4 anti-melanoma antibodies to screen first/second type (e.g. healthy/unhealthy) individuals forming "fifth" and "sixth" products, respectively. See Abstract; examples.

23. Applicant's arguments filed on 7/29/05, regarding the anticipatory rejection of claims over Cai et al have been fully considered but they are not persuasive.

Note the amended claim 1 method steps do not require both second product and fourth product to identify the polypeptides present in the first and second biological samples. According to the claims 'wherein the presence or absence of a species in said second product or fourth product is indicative of the identity of the polypeptide that is present in said first and second complex biological samples....' Thus, according to the method only either method steps c) to d) or method steps e) to f) are required to identify the polypeptide.

Applicants traverse the rejection. Applicants assert that 'one key feature of the instant method is that the same peptide-nucleic acid coupled library is first independently exposed to polypeptides from two samples.'

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the instant method is that the same peptide-nucleic acid coupled library is first independently exposed to polypeptides from two samples) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants assertions are not persuasive, because according to the instant claimed method steps the PNA-coupled library is not exposed to polypeptides of different samples, i.e., the PNA-coupled library is exposed to the first array to form first product (step c); and then exposing the first product to second array (step d).

Further, applicants argue that Cai only exposes melanoma cells to a single phage library and members of the library that were eluted from the same melanoma cells. Cai does not expose the melanoma cells to phage eluted from another sample that was contacted with the entire phage library.

Applicants arguments are not persuasive, because Cai et al teach the library was screened against the live cultures of tumor (refers to the first complex of biological sample); and the panned phage (selected or identified or first product) (refers to the instant claim step c) is again exposed to normal melanocytes (refers to the second array of the instant claims) (refers to the instant claim step d) to enrich for antibodies which react with melanoma cells (refers to the instant claim second product). And further the unabsorbed phage (refer to step e) of the instant claims) are tested against several different samples, which would refer to the subsequent products of the instant claims.

The new claim 54 is included in this rejection because Cai et al teach testing the library in healthy and non-healthy individuals (refers to different subjects). Thus, for the reasons of record the rejections have been maintained.

24. Claims 1-11, 17, 19, 20, 23-27, 29-48, 50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cai et al. PNAS USA Vol. 92, pages 6537-6541 (July 1995) and Hutchens et al. US Pat. No. 6,225,047 (5/01: effectively filed 6/97).

Cai et al. teach a method for identifying a "polypeptide" (e.g. antibodies or antigen markers of normal vs tumor (e.g. melanoma) cells by adhering (e.g. culturing) "complex biological samples" (e.g. cells) from normal (e.g. healthy melanocytes) vs abnormal (e.g. tumor cells) (e.g. corresponds to steps a and b of present claim 1. Anti-

melanoma antibodies were selected from each library by panning the phage against live cultures of the autologous tumor (e.g. from a "first type of individual" e.g. unhealthy)in which the complexed antibodies corresponding to a "first product" . The panned phage population was extensively absorbed against normal melanocytes (e.g. "biological sample from a second type of individual e.g. healthy) to enrich for antibodies that react with melanoma cells but not with melanocytes (e.g. unabsorbed antibody library as "second product") which anticipated present claims 1, 8-11, 17, 19, 20, 23-24 . The unabsorbed phage were amplified/cloned and tested (e.g. ELISA)against (e.g. exposing the library):

a. "a complex biological sample from a second type of individual i.e. healthy such as normal endothelial and fibroblast cells) to identify antibodies that bind or those that don't (either of which corresponds to "a third product"); and

b. "a complex biological sample from a first type of individual i.e. unhealthy such as melanocytes, several melanoma lines and eight other tumor lines) to identify antibodies that bind or those than don't (either of which corresponds to a "fourth product" but especially those that bind tumor antigens. thus anticipating present claims 2 (and claims dependent thereon). The reference teaches evaluating the test results of the above ELISA's , including those of the "second" and "fourth" products (e.g. anticancer i.e. anti-melanoma antibodies) thus anticipating claim 3. The reference further teaches the identification (e.g. by ELISA) of different (e.g. three) classes of anti-melanoma antibodies from different patients; and the ***repeating of the above procedures*** utilizing the newly found anti-melanoma antibodies to screen the antibody repertoire of any

person with cancer (or a person without cancer) which anticipates present claims 4-7 e.g. pooling and amplification of the product 2/4 anti-melanoma antibodies to screen first/second type (e.g. healthy/unhealthy) individuals forming "fifth" and "sixth" products, respectively. See abstract; examples.

Cai et al. Reference teaching differs from the presently claimed invention by failing to disclose:

a. the use of a solid support with cross-linker attachment of analyte (e.g. claims 29-32);

b. use of mass spectrometry to analyze products (e.g. claims 37-41).

However, Hutchens teaches the favorable use of "rententate chromatography" which includes cross-linking analytes to solid supports and determining products by mass spectrometry when evaluating product components in assays involving different tissues (including healthy vs. diseased) and phage capture. See e.g. Figures 1-33 (especially figures 13-18; figures 21-29); col. 4 (especially lines 30-40; col. 5 (especially lines 40-45); col. 9, lines 10-50; col. 18-20; col. 36; examples and patent claims.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to modify the Cai reference method to cross-link analytes to solid supports and use mass spectometry to analyze products in order to optimize the Cai phage screening of tissue components in an analogous manner as in the Hutchen's reference.

25. Claims 1-11, 17, 19, 20, 23-48, 50 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cai and Hutchens et al. as applied to claims 1-11, 17, 19, 20, 23-27, 29-48, 50 and 52 above, and further in view of Cull et al., Methods in Enzymology Vol. 182:147-238.

Cai et. al. and Hutchens Reference teachings described above in the obviousness rejection is hereby incorporated by reference in its entirety. The Cai et al teaching separately, or combined with Hutchens, differs from the presently claimed invention by failing to teach denaturation of the complex biological sample prior to adhering to a support to create an array (e.g. claim 28).

However, Cull et al. teaches that preliminary processing of biological samples, including the use of preliminary separation techniques and/or denaturation, may be desirable in order to effect better analyte (e.g. peptide) purifications and/or use in subsequent screening.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to incorporate a denaturation step into the Cai method (or when combined with Hutchen) prior to attachment and/or adherence of the biological sample to the support in order to optimize analyte purification and/or its subsequent screening.

26. Applicant's arguments filed on 7/29/05, regarding the obviousness rejections (note both the rejections argued together) have been fully considered but they are not persuasive.

Applicants argue that Cai does not teach or suggest limitations in the independent claims. And teachings of Huchens on using cross-linkers or mass spectrometry or Cull on preliminary processing of biological samples do not remedy the deficiencies of Cai.

Applicants arguments have been considered and are not persuasive. Applicants arguments regarding the teachings of the Cai has been addressed supra, which would be applicable to the current obviousness rejections. New claim 54 is included in these rejections because Cai et al teach testing samples from two different individuals (healthy and unhealthy). Thus, the rejections of record have been maintained for the reasons of record.

Conclusion

27. No claims are allowed.

28. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

PADMASHRI PONNALURI
PRIMARY EXAMINER

14 October 2005